

1. Essential Prescribing Information

The CoreTherm system is a patented device for treatment of BPH by delivering microwave energy to the prostate. The system comprises a mobile control unit, a transurethral catheter, a microwave antenna, an intraprostatic temperature probe, a rectal temperature probe and a penis safety probe. A laptop computer displays all treatment parameters, including the measured intraprostatic temperature, calculated intraprostatic blood flow and calculated tissue necrosis. Based on this information the operator can adjust the microwave power and treatment time manually to achieve desired intraprostatic temperature (preferably 50-60°C).

This manual contains essential information for operation of the CoreTherm microwave thermotherapy system. A description of the equipment, including function, set-up, operation procedures and heating pattern is also provided in this manual. This information is intended to provide clinical guidance when using the CoreTherm microwave system for BPH thermotherapy treatments.

This manual contains the following sections:

- Essential Prescribing Information
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- Brief Device Description
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- Warnings
- Precautions
- Adverse Events
- Clinical Studies
- Individualization of Treatment
- Patient Counseling Information
- Standards
- How Supplied
- Operator's Manual
- Patient Information

Caution

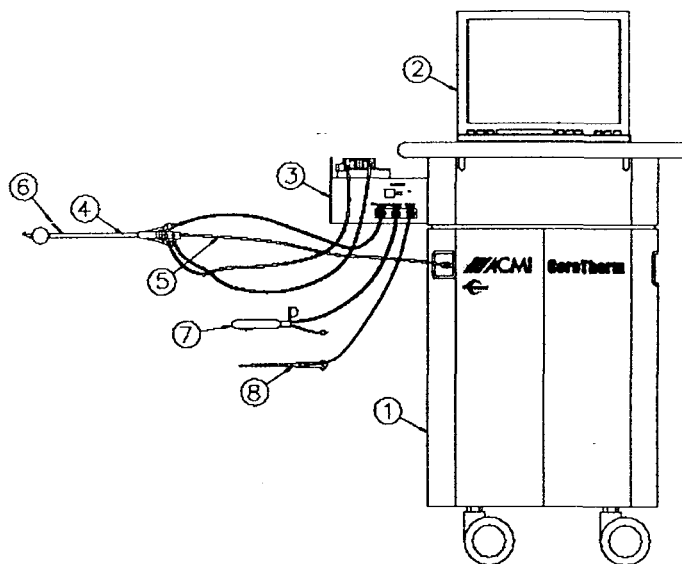
Federal (U.S.A.) law restricts this device to sale by or on the order of a physician trained in the use of this device.

The CoreTherm system must only be used by qualified operators upon the prescription and under the supervision of a physician who is experienced in clinical thermotherapy and in accordance with the instructions in this manual.

Instructions for Use

CoreTherm System Description

The CoreTherm system is an operator-controlled device designed to deliver microwave energy to the prostate. The CoreTherm system includes the following parts:



The CoreTherm system comprises:

- 1 CoreTherm Control Unit
- 2 Laptop PC with CoreTherm SW Pac
- 3 Pull Out Drawer
- 4 CoreTherm Catheter
- 5 Microwave Antenna
- 6 Intraprostatic Temperature Probe
- 7 Rectal Temperature Probe
- 8 Penis Safety Probe

The device has four wheels and a handle for easy transportation of the equipment. The two front wheels have integrated brakes which are applied and released by the operator. The CoreTherm device only requires an external grounded electrical outlet. During treatment, the microwave antenna is used to heat the prostate tissue. The actual intraprostatic temperature is continuously measured by the intraprostatic temperature probe. A transurethral catheter holds the antenna and the intraprostatic temperature probe in place during the treatment. The heating process is controlled by the operator, who continuously monitors the temperature measured by the intraprostatic temperature probe. The operator adjusts the microwave power accordingly. To ensure safe treatment and avoid overheating, the system continuously monitors the rectal temperature and penile skin temperature at the penoscrotal angle. All important treatment variables such as intraprostatic temperature, calculated cell-kill, intraprostatic blood flow and microwave power are displayed on the computer screen throughout the entire treatment session.

CoreTherm Control Unit

The CoreTherm control unit includes a microwave generator, a temperature recording system, a water circulation system and computer-controlled delivery of microwave energy to the prostate while continuously monitoring the intraprostatic temperature.

Laptop PC

A laptop PC with the PLFT Software is connected to the control unit of the CoreTherm system. The software handles the user interface and allows the operator to register patients and set treatment parameters. It also displays treatment information, such as intraprostatic temperatures and safety temperatures, continuously during the treatment. . .

For detailed technical data, see See Appendix C – CoreTherm Technical Specifications.

Microwave Antenna

The Microwave Antenna, with the radiating part, directs the microwave radiation into the prostate tissue. The Microwave Antenna is delivered in a separate package. The Microwave Antenna is inserted into the treatment catheter and secured with a luer lock. The Microwave Antenna must be fitted into the CoreTherm catheter prior insertion into the patient.

The design provides a narrow and focused heating pattern.

The Microwave Antenna is designed to be used in prostates ≥ 35 mm in length. Use the Microwave Antenna only 10 times.

For detailed technical data, see See Appendix C – CoreTherm Technical Specifications.

CoreTherm Catheter

The CoreTherm catheter is primarily used to house the microwave antenna and the intraprostatic temperature probe during treatment. Water is circulated through the CoreTherm catheter in order to remove heat losses from the microwave antenna cable. The CoreTherm catheter has a balloon close to its tip. The balloon is inflated during treatment to keep the catheter anchored at the bladder neck.

The CoreTherm catheter, the water tubes, and the water bag are permanently assembled and no attempt should be made to disassemble them. The CoreTherm catheter is provided sterile and is intended for single use.

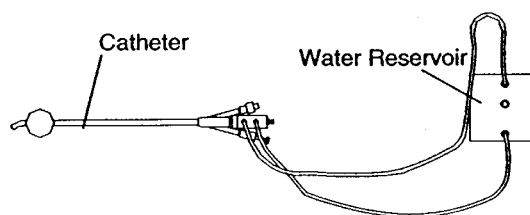


Illustration of the CoreTherm Catheter.

Intraprostatic Temperature Probe

The intraprostatic temperature probe records the intraprostatic temperature during treatment.

The probe is secured to the catheter with a luer lock. The intraprostatic temperature probe has three temperature sensors located at the tip of the probe with gaps of 10 mm between each sensor. An additional fourth sensor is placed further back in the intraprostatic temperature probe to measure the temperature of the circulating water that is used to remove heat losses from the Microwave Antenna cable.

Rectal Temperature Probe

The rectal temperature probe records the rectal temperature during treatment. If the temperature exceeds the safety limit (preset to 43°C), the microwave generator's output will be shut off automatically. The rectal temperature probe contains three temperature sensors and a balloon. The balloon can be inflated with 0 to 5 ml air during treatment if needed to keep the rectal temperature probe in place. The temperature sensors are located at the tip of the probe, against the inner, anterior rectal wall.

Penis Safety Sensor

The penis safety probe records the skin temperature at the penoscrotal angle during treatment. If the temperature exceeds the safety limit (preset to 40° C), the microwave generator's output will be shut off automatically. The penis safety probe contains a temperature sensor and should be fastened at the base of the penis, with the sensor at the penoscrotal angle.

Indications for Use

The ProstaLund® CoreTherm™ is a non-surgical, minimally invasive, device intended to relieve symptoms associated with symptomatic Benign Prostatic Hyperplasia (BPH) by ProstaLund Feedback Treatment® (PLFT®), and is indicated for men with a prostate size of 30-100 g and prostatic urethra length > 35 mm.

Contra-indications

The contra-indications for PLFT are:

- Severe urethral stricture preventing easy catheterization;
- Patients with penile or urinary sphincter implants;
- Previous radiation of pelvic region;
- Prostate size < 30 g; prostate length < 35 mm;
- Clinical or histological evidence of bladder cancer;
- Active prostatitis;
- Active urinary tract infection;
- Previous prostate or rectal surgery;
- Interest in the preservation of fertility;
- Implanted defibrillators, pacemakers or any other active implant;
- Metallic implant in the prostate treatment area;
- Peripheral arterial disease with intermittent claudication.

Warnings

The following is a list of warnings for safe and effective operation of the CoreTherm system.



Warning – Patient Safety

PLFT (ProstaLund Feedback Treatment) has inherent risks of complications (refer to Adverse Events). The CoreTherm system and components should not be used in any way other than in accordance with the intended use, indications for use and instructions for use. Failure to do so could result in compromised patient safety and/or result in insufficient therapy.



Warning – Damage to the External Sphincter

If the CoreTherm catheter is incorrectly placed or moves during treatment, the patient's external sphincter may overheat, causing temporary or chronic incontinence. Use ultrasound to verify that the CoreTherm catheter is correctly positioned, and check the position of the catheter regularly during the treatment to ensure that it has not moved.

Precautions

The following is a list of precautions for safe and effective operation of the CoreTherm system.

Therapy Related – Before Treatment

Caution – Direct Supervision

The use of the CoreTherm system must be prescribed and administered under the direct supervision of a qualified and trained physician, after appropriate medical evaluation of the patient.

Caution – Recommended Tissue Necrosis

Before starting a PLFT session, it is important that the presiding physician decide how much tissue to necrose. The following table offers recommendations according to clinical experience:

Table 1:

Prostate Weight (g)	Recommended tissue necrosis
< 30	not suitable for PLFT
≥ 30 and ≤ 40	15% – 20%
> 40 and ≤ 60	20%
> 60 and ≤ 100	30%

Caution – Patient Information

Before treatment a responsible physician must ensure that the patient has read the patient information. It is also important for the patient to be given information verbally, with an explanation of how the treatment is to be performed and what to expect during and after treatment.

Caution – Over-Sedation of the Patient

Do not over-sedate the patient. The patient's perception of pain is an important safety mechanism to ensure that excessive heat is not applied to the tissue. Do not administer a general or spinal anesthetic.

Caution – Improper Insertion of the CoreTherm Catheter

Exercise care when inserting the CoreTherm catheter into the patient's urethra. Perforation and subsequent infection of the urethra may occur.

Caution – Reuse of Temperature Probes and Antenna

Always check for how many procedures the temperature probes and microwave antenna have been used before starting a new treatment. Recommended reuse life is 10 times. To check number of uses, select Probe and Antenna statistics under the Tools menu.

Caution – Incorrect Positioning of the Intraprostatic Temperature Probe

If the intraprostatic temperature probe is incorrectly positioned in the patient's prostate, the temperature feedback may be inaccurate. This could result in the application of insufficient or excessive heat to the prostate. Ensure that the intraprostatic temperature probe is correctly positioned. If necessary, use transrectal ultrasound (TRUS) to verify if the probe is correctly positioned.

Caution – Patient Injury

The use of damaged equipment may injure the patient. When preparing the patient for treatment, always check the intraprostatic temperature probe, the rectal temperature probe, the penis safety probe and the microwave antenna for cracks or any sign of physical damage. Exchange any damaged item for a fully operational, undamaged item before initiating the treatment.

Caution – Use only Sterile Water

Use only sterile water to fill the catheter balloon. Do not use saline. Using saline may cause interaction between the microwaves and the ions in the solution that could cause the CoreTherm catheter to overheat.

Caution – Reuse of the CoreTherm Catheter

The CoreTherm catheter is intended for single use only. Reuse may result in an unsafe treatment and/or contribute to cross-contamination between patients.

The CoreTherm catheter is a disposable and a unique treatment number is required for each treatment. The software includes a lock that prevents reuse of the treatment number. Do not attempt to use a treatment number for more than one treatment session.

Caution – Verify Catheter Placement

Always verify the position of the CoreTherm catheter (balloon) by performing an ultrasound examination before treatment is started.

Caution – Cleaning Agents

The use of cleaning agents other than those stipulated in the cleaning instructions may cause damage to the equipment. Follow the instructions given in this manual when reprocessing reusable components of the CoreTherm system.

Caution – Insufficient Cleaning / Sterilization

Ensure that all temperature probes and the microwave antenna are properly cleaned, disinfected and/or sterilized before use in accordance with the instructions given in this manual, otherwise infection may result.

Caution – Probe Calibration

The accurate measurement of treatment and safety temperatures is critical for performing safe and effective treatments. Incorrectly calibrated temperature probes will result in erroneous temperature readings that may jeopardize the safety of the patient and cause permanent injury. Follow the calibration instructions given in this manual.

Caution – Hot Surfaces

During calibration the surfaces of the calibration oven in the pull out drawer of the CoreTherm control unit are hot. The temperature probes are also hot during and after calibration. Do not touch the hot surfaces of the probes or the calibration oven. Exercise caution when calibrating the temperature probes as burn injuries may result. Do not place foreign objects or insert fingers into the oven.

Caution – Liquid Ingress

Do not allow the CoreTherm control unit or the laptop computer to get wet as permanent damage may occur.

Caution – Care of Accessories

CoreTherm accessories must be stored, handled and sterilized according to the Instructions given in this manual and must never be exposed to temperatures over 80°C as permanent damage may occur.

Therapy Related – Treatment

Caution – Injury to Operator

Use caution when opening and closing the pull out drawer of the CoreTherm control unit to prevent injury to the operator.

Caution – Overturning the Control Unit

Do not tilt the CoreTherm control unit from the upright position. Tilting could cause the unit to overturn and cause injury to the staff, patient and damage to the unit.

Caution – Damage to Connectors

Do not attempt to close the pull out drawer of the CoreTherm control unit when probes are attached as damage to the connectors may result.

Caution – Remain with the Patient

The responsible physician must remain with the patient and supervise the treatment.

Caution – Overheating of the Prostate Tissue

To avoid the risk of burn injuries to the bulbar urethra or the external sphincter, the temperature of the CoreTherm catheter is measured by a sensor placed 138 mm from the catheter tip. This is located approximately midway between the penis and the external sphincter. Microwave power is shut down if this temperature exceeds 40°C.

Caution – Excessive Rectal Temperature

To avoid the risk of fistulas, the rectal temperature during treatment should not exceed 43°C. The microwave power will shut off if the rectal temperature exceeds preset limits. You must monitor the rectal temperature and check the position of the probe regularly throughout the treatment.

Caution – Excessive Temperature at the Penoscrotal Angle

There is a risk of burn injuries to the penis and urethra if the CoreTherm catheter moves during the treatment or if the penile temperature exceeds the safety limit. To avoid this risk microwave power will shut off if the penis safety probe exceeds 40°C. You must regularly monitor the penile temperature and check the position of the catheter throughout the treatment.

Caution – Overheating of the CoreTherm Catheter

The CoreTherm catheter can overheat if the CoreTherm catheter malfunctions or is damaged. This could lead to thermal damage to the external sphincter or bulbar urethra. The temperature of the circulating water is measured by one of the sensors in the intraprostatic temperature probe. If the temperature of the circulating water exceeds the preset safety limit of 40°C, the microwave power is shut off. Monitor the temperature of the circulation water regularly throughout the treatment.

Caution – Minimum Prostate Weight / Length

Do not use the CoreTherm system to treat patients whose prostate is less than 30 g in weight and/or less than 35 mm in length, otherwise injury to the patient may result.

Caution – Prostate cancer or prostate weight >100 g

The safety and efficacy of PLFT in patients with prostate cancer or in patients with prostate weight >100 g have not been investigated.

Caution – Incompatible Equipment and Software Programs

- The CoreTherm system may malfunction if transmitting devices such as mobile telephones or two-way radios are used near the equipment.
- Do not install any other software on the computer as this may cause the CoreTherm system to malfunction.
- You must quit all other applications/programs before starting the PLFT Software. Do not attempt to run other applications simultaneously as this may impair the correct functioning of the unit.
- Do not adjust or replace the operating system of the computer as this may impair the correct functioning of the unit. All setup and configuration of the software must be performed by authorized service personnel.

Caution – Loss of Data

If the unit is switched off while the program is accessing the hard drive, data may be lost or corrupted. To prevent loss or corruption of data, always quit the program prior to turning off the unit. Data should be backed up routinely.

Therapy Related – Post Treatment

Caution – Insufficient Retraction of the Intraprostatic Temperature Probe

Insufficient retraction of the intraprostatic temperature probe into the CoreTherm catheter before the catheter is removed may cause injury to the patient. It is therefore important to retract the intraprostatic temperature probe at least 50 mm before the CoreTherm catheter is removed.

Caution – Use of the Suprapubic Drainage

Always use an indwelling urethral catheter after treatment. Use of suprapubic drainage may risk permanent occlusion of the urethra.

Caution – Increased PSA Levels

Prostate specific antigen (PSA) levels will increase significantly in the first three months after treatment. The results of PSA testing during this period are therefore unreliable.

Caution – Administer a Prophylactic Antibiotic

It is recommended that a prophylactic antibiotic should be administered in accordance with the clinical routines of the department. For the first week after CoreTherm treatment it is important for the patient to avoid excessive physical exertion.

Caution – Catheterization Period

It is recommended that patients remain catheterized (with indwelling catheter), for 1 to 3 weeks after treatment. Patients often experience urgency during the first period after treatment. This will diminish gradually, although it is not unusual for the feeling to persist for up to a month.

Caution – Removal of the Catheter

After removal of the catheter, a small risk of urine retention is still present, it is therefore important to maintain contact with the patient at this time.

Caution – Tissue sloughing

During the first few months after treatment it is not unusual for small pieces of necrotic tissue or small amount of blood to be discharged with the urine. This is due to the destruction of the prostatic urethra during treatment.

Caution – Safety and Effectiveness of Retreatment

The safety and effectiveness of retreatment with the CoreTherm system has not been established.

Device Related – Microwave and AC Power

Caution – 915 MHz Operating Frequency

The CoreTherm system complies with the requirements of the publication IEC601-1-2:1993, with the exception of the 915 MHz frequency, which is the operating frequency of the unit. In region 2 (including USA), 915 MHz is an unrestricted frequency.

Caution – Power Requirements

The CoreTherm unit must be plugged into the appropriate voltage outlet.

Power requirements:

Voltage:

- 100 V to 120 V at 50 Hz or 60 Hz
- 220 V to 240 V at 50 Hz or 60 Hz

Fuses:

- 2 x 10 A, slow blow (100 V to 120 V)
- 2 x 6.3 A, slow blow (220 V to 240 V)

Caution – Installation and Testing

The CoreTherm system must be installed and tested prior to use by a factory authorized representative.

Caution – Voltage and Cabling

Ensure that the voltage indicated by the label on the side of the CoreTherm system matches the available voltage.

Use only the electrical power cable supplied with the CoreTherm system. This cable must be fitted with a hospital approved three-pole plug with a protective ground conductor.

Never use an extension cable with the main electrical power cable. The length of the extended cable increases the resistance of the protective ground conductor beyond an acceptable level.

Always keep power cables, sockets and plugs clean and dry.

Caution – Grounding System

The equipment may only be connected to an AC power supply that has a protective ground conductor in accordance with IEC requirements or applicable local regulations. The grounding system in the treatment area should be checked regularly by a qualified engineer or hospital safety personnel.

Any interruption of the protective earth conductor inside or outside the equipment, or disconnection of the protective earth terminal, are likely to make the apparatus dangerous. Intentional interruption is prohibited. The ground conductor must be checked regularly.

Caution – Lethal Voltages

Lethal voltages are present in this equipment when it is connected to the electrical supply. Disconnect the equipment from the electrical supply before removing the covers or attempting any service or repair activity, otherwise death or personal injury may result.

Caution – Danger of Electrical Shock

Do not connect a printer or other external electrical equipment to the CoreTherm unit during treatment. This may compromise the electrical insulation of the patient from the electrical supply. A printer may only be connected when the laptop is disconnected from the CoreTherm unit.

Caution – Potentially Explosive Environments

The CoreTherm system is not designed for use in potentially explosive environments. It must not be operated in the presence of flammable liquids or gases.

Caution – Danger of Microwave Radiation

Microwave power may only be emitted when the CoreTherm catheter and/or the microwave antenna are correctly positioned within the patient's body. Otherwise injury to the patient and/or the operator may result.

Caution – Distance to Other Medical Devices

The CoreTherm system may disturb the operation of other medical devices. In order to minimize this, a separation distance of at least 3 feet (1 meter) from the CoreTherm unit, including cables should be maintained.

Caution – EMC precautions

The CoreTherm unit needs special precautions regarding EMC and needs to be installed and put into service according to the EMC information provided in this manual.

Caution – RF Communications

Portable and mobile RF communications equipment can affect the CoreTherm system and should not be operated in the same area at the same time the CoreTherm unit is in use.

Caution – Cable Length

The electrical cable length shall not exceed 9 feet (3 meters).

Caution – Accessories, Transducers and Cables

The use of accessories, transducers and cables other than those specified, with the exception of transducers and cables sold by the manufacturer of the CoreTherm system as replacement parts for internal components, may result in increased emissions and decreased immunity of the CoreTherm system.

Caution – Placement of Equipment

The CoreTherm unit shall not be used adjacent to or stacked with other equipment. If the operator deems adjacent or stacked use as necessary, the CoreTherm unit shall be observed to verify normal operation in the configuration in which it is use.

Caution – Emission Levels and Degree of Immunity

The use of accessories and cables, other than those stated in the instructions given in this manual and provided by ProstaLund may result in increased emissions or decreased immunity of the CoreTherm system.

CoreTherm Quick Reference Guide

This guide is designed to provide a Quick Reference and not to replace the User's Manual. Please refer to the User's Manual for complete instructions on Operation and Patient Preparation.

Patient Preparation

- 1 Position patient so that he is comfortable in a supine position or Semi-Fowler's position.
- 2 Prepare the treatment catheter and the temperature sensors. Insert the antenna into the treatment catheter and tighten luer lock (Do not lubricate the antenna). Fill the water chamber with 75cc sterile water (Do not use saline) using a Toomey syringe. Insert the IP probe into the catheter fully to determine position, and then retract until tip is visible inside the opening, but not protruding.
- 3 Prepare and drape the genital area.
- 4 Insert local anesthetic into the urethra and clamp penis with a penis clamp to retain the jelly in the urethra. Wait at least 5 minutes.
- 5 Insert a straight catheter to drain the bladder.
- 6 Before inserting the CoreTherm catheter, administer another dose of local anesthetic into the urethra.
- 7 Insert the assembled treatment catheter. The catheter should be fully inserted with the tip pointing upwards. Inflate the balloon with 20cc of sterile water.
- 8 Gently withdraw the catheter until the balloon rests at the bladder neck.
- 9 Alert the patient that he might feel a stick. Gently pull on the catheter to straighten and insert the intraprostatic temperature probe. Check the position of the catheter (balloon) by performing an ultra-sound examination.
- 10 Cover the rectal probe with a condom, lubricate the outside of the condom and insert into the rectum with the handle pointing upwards. Secure the position of the rectal probe with a rolled towel.
- 11 Secure the penile safety sensor around the base of the penis at the peno-scrotal junction. Make sure the temperature sensor is positioned at the base where it is closest to the urethra.
- 12 Connect the antenna, IP temperature sensor, rectal temperature sensor and penis safety sensor to the control unit.
- 13 Position the long water tube from the catheter in the pump housing and lock in place.
- 14 Before starting the treatment ensure that the antenna cable is secured to the catheter. Confirm correct positioning of all safety sensors and the treatment catheter. You are now ready to start the treatment. Do not cover the patient's genitalia. The patient must be monitored to confirm that the catheter and probes have not been displaced during treatment, or that there is water leakage from the catheter.

Performing the Treatment

- 1 The PLFT software starts automatically when the laptop computer is turned on. If needed the PLFT software can also be started manually by clicking on the PLFT SW icon on the desktop. Login using your User Name and Password. (Refer to the User's Manual if you have forgotten your password). Click on Log In.

- 2 Click on PLFT, then Patient List. Click Patient, then Add Patient. You are required to enter first and last name and an ID code. Optional fields are available. Click on Save when ready.
- 3 Click on the correct patient from the Patient List. Click on PLFT Treatment, then New Treatment. Confirm that Treatment Settings shows correct name and ID code of selected patient.
- 4 Enter length and weight of the prostate as determined by TRUS. Prostate length is a required field. Alternatively, enter length, width, height of the prostate and the PLFT system will calculate the weight automatically.
- 5 Enter the Operator from the list, or type name into field.
- 6 Enter antenna serial number and catheter number (also called treatment code) into appropriate fields. Click on Continue.
- 7 Confirm information and click OK.
- 8 The treatment page opens and the pump starts circulating water.
- 9 Check temperature readings and confirm that they are logical, prior to starting treatment. (IP probe 35-37°C, rectal 35-37°C and penis safety 28-35°C). The blood flow index will not be displayed for several minutes after treatment is started.
- 10 Adjust default temperature limits and treatment duration, if desired. Click Setup tab, use arrows to adjust, click Apply. Refer to User's Manual for other settings.
- 11 Click Start to begin treatment and select power.
- 12 Monitor the temperature screens and the blood flow (when it becomes available). Determine the desired amount of cell kill and observe progress on screen. Adjust power as needed to maintain temperatures and get desired cell kill.
- 13 Adjust Stub Tuner as needed to maintain reflection below 1.0 W. Click on Stub Tuner, then Semi-Auto for simple automatic adjustment. Refer to the User's Manual for Manual Adjustment.
- 14 Stop treatment when desired cell kill is achieved by clicking Quit.
- 15 Retract IP probe so that it resides inside the catheter (at least 2 inches), deflate catheter balloon and remove catheter and all probes / sensors. Immediately insert a Foley catheter (urethral edema happens quickly and may result in difficult catheter insertion if delayed).
- 16 Instruct the patient in post-treatment expectations and catheter care. Discharge when ready.

Post-treatment Care of Equipment

- 1 Remove condom from rectal probe and discard condom. Wipe rectal probe with an enzymatic detergent solution and dry.
- 2 Use a soft cloth and an enzymatic detergent to clean the penis safety sensor, antenna and IP probe. Rinse well and dry. Antenna, rectal probe and penis safety sensor should be disinfected.
- 3 Sterilize the IP probe prior to use in the next patient.
- 4 Refer to the User's Manual for cleaning, disinfection and sterilization procedures.

Adverse Events

A total of 183 patients in three studies were treated with PLFT and evaluated in the clinical investigation. In all three studies the patients were treated once with PLFT: in Study A, 100 patients were treated; in Study B, 42 patients were treated; in Study C, 41 patients were treated. The vast majority of adverse events after PLFT emanated from the urinary tract system. In most cases, the events were of mild or moderate intensity. A single patient may report several different adverse events.

The treatments were performed with twelve (12) different ProstaLund® control units. No deaths were reported assessed by the investigator as probably or possibly related to PLFT. No patient was discontinued from the study due to a device-related adverse event. Patients with symptoms of urinary tract infection recovered with antibiotics following treatment.

The following table identifies the adverse events reported in the three studies. The PLFT columns represent pooled adverse event data from study A, B and C. The column for the TURP group presents pooled data from study A and B.

Table 2:

At Treatment	Number PLFT	Rate PLFT	Number TURP	Rate TURP
Urgency	19	10.4%	1	1.5%
Suprapubic and General Pain including Penile Pain	12	6.6%	0	0.0%
Bladder Spasm	7	3.8%	0	0.0%
Hypertension	4	2.2%	0	0.0%
Hypotension	4	2.2%	1	1.5%
Bleeding	2	1.1%	0	0.0%
Impotence*	1	0.5%	0	0.0%
Hematuria	1	0.5%	1	1.5%
Dysuria	1	0.5%	0	0.0%
Hemorrhage non-specific	0	0.0%	5	7.7%
Urinary Incontinence	0	0.0%	2	3.1%
Urinary Tract Infection	0	0.0%	1	1.5%
Post-operative hemorrhage	0	0.0%	1	1.5%
Neoplasm non-specific	0	0.0%	1	1.5%
Chest pain	0	0.0%	1	1.5%

Day 2-5	Number PLFT	Rate PLFT	Number TURP	Rate TURP
Bladder Spasm	10	5.5%	0	0.0%
Urgency	6	3.3%	2	3.1%
Urinary Retention	3	1.6%	4	6.2%
Dysuria	2	1.1%	0	0.0%
Hematuria	2	1.1%	1	1.5%
Suprapubic and General Pain including Penile Pain	2	1.1%	0	0.0%
Micturition Frequency	1	0.5%	0	0.0%
Bleeding	1	0.5%	0	0.0%
Epididymitis	1	0.5%	0	0.0%
Urinary Tract Infection	0	0.0%	4	6.2%
Urinary Incontinence	0	0.0%	3	4.6%
Post-operative hemorrhage	0	0.0%	1	1.5%
Neoplasm non-specific	0	0.0%	1	1.5%
Chest pain	0	0.0%	1	1.5%

Day 6 to 1 Month	Number PLFT	Rate PLFT	Number TURP	Rate TURP
Urgency	25	13.7%	3	4.8%
Urinary Retention	22	12.0%	4	6.3%
Bladder Spasm	17	9.3%	0	0.0%
Urinary Tract Infection	13	7.1%	5	7.9%
Dysuria	10	5.5%	0	0.0%
Hematuria	6	3.3%	5	7.9%
Micturition Frequency	3	1.6%	0	0.0%
Suprapubic and General Pain including Penile Pain	3	1.6%	0	0.0%
Epididymitis	2	1.1%	1	1.6%
Urinary incontinence	2	1.1%	3	4.8%

Day 6 to 1 Month	Number PLFT	Rate PLFT	Number TURP	Rate TURP
Post-operative hemorrhage	1	0.5%	4	6.3%
Neoplasm non-specific	1	0.5%	2	3.2%
Impotence*	2	1.1%	2	3.2%
Ejaculation disorder	0	0.0%	1	1.6%
Urethral stricture	1	0.5%	1	1.6%

* Impotence is relatively common in this patient category and may occur unspecifically after any urological intervention. There is no evidence of impotence being associated with PLFT.

Adverse Events at Treatment until 1 Month

All patients in the PLFT group were discharged with an indwelling catheter. The mean post-treatment indwelling catheter time was 14, 20, and 18 days for the PLFT group in the A, B, and C studies, respectively. As seen in the table above, urgency and bladder spasm was the major adverse event seen during the time period. Suprapubic/general pain and penile pain were reported during treatment, but thereafter in a considerably lower frequency. A few cases of hypertension or hypotension occurred during treatment. Dysuria, hematuria, bleeding and micturition frequency were reported occasionally. During Day 6 to 1 month post treatment urinary retention and urinary tract infection were relatively common. There were two cases of epididymitis and urinary incontinence (1.1% of patients).

In the TURP group, i.e. the patients treated with TURP in the A and B studies, urinary incontinence and urinary tract infection were relatively common during the time period. At the day of treatment also hemorrhage non-specific was reported (7.7%). During Day 6 to 1 month hematuria (7.9%) and postoperative hemorrhage (6.3%) were the most common adverse events.

Adverse Events 1 Month until 3 Months

Urgency and urinary tract infection was reported for 24 patients (13.1%) in the PLFT group. Bladder spasm and urinary retention were decreasing in frequency compared to the previous time period and was reported for 9 patients (4.9%). Dysuria, hematuria, micturition frequency, prostatitis, ejaculation disorder (i.e. retrograde ejaculation) and impotence were reported occasionally (4.4%, 2.2%, 1.6%, 1.1%, 1.1% and 1.1% of patients, respectively). The same was true for epididymitis and urinary incontinence (2.2% and 1.6% of patients, respectively).

In the TURP group urinary incontinence (9.5%) and urinary tract infection (6.3%) were still rather common. Urgency was experienced by 7.9% of the patients, while impotence was reported by 4.3%.

Adverse Events After 3 Months Post-Treatment

There were 181 patients available for follow-up in the PLFT group during this time period. The tendency for urgency and urinary tract infection was lower as compared to the previous time period (7.7% and 6.6%, respectively). Bladder spasm and urinary retention were uncommon (2.2% of patients), as well as hematuria, micturition frequency, and prostatitis (1.7% of patients). There were a low number of patients with urinary incontinence (3.3%), urethral stricture (2.2%), and epididymitis (1.7%). Three cases of bladder calculus (1.7%) has been reported. Both impotence and ejaculation disorder were reported for 9 patients (4.9%). Ejaculation disorder (i.e. retrograde ejaculation) is anticipated to occur to a certain extent.

Urgency and urinary incontinence were still rather common and reported by 10.3% and 8.6% of the patients in the TURP group, respectively. The cases of impotence increased to 8.6% and ejaculation disorder were reported by 6.9%.

Duration of Adverse Events

Urgency, bladder spasm, and urinary tract infection had all a median duration of 11 days. Urinary retention was treated successfully, generally with placement of a catheter, and median duration of the event was one day. Suprapubic and general pain including penile pain had also a median duration of one day. Hematuria and bleeding had median duration of 1 and 3 days, respectively, and dysuria 19 days. Micturition frequency, prostatitis, urinary incontinence, urinary stricture, and epididymitis had intermediate duration, and were typically resolved within 22, 29, 99, 51, and 33 days, respectively (median values).

In comparison, urgency in the TURP group had a median duration of 73 days, urinary incontinence lasted typically 165 days and urinary tract infection 20 days. Hematuria, urinary retention, hemorrhage non-specifics and post-operative hemorrhage were resolved within a few days; 3 days, 1.5, 1 and 1 day respectively.

At 12 months ongoing adverse events were few in the PLFT group. There was one patient (0.5%) each with bladder spasm, hematuria, prostatitis, pain, or urinary tract infection, two patients (1.1%) with micturition frequency, urgency, or urethral stricture, and 3 patients (1.6%) with urinary incontinence. In addition there were 9 patients each with impotence and ejaculation disorder (4.9%) ongoing at 12 months.

Ongoing adverse events after 12 months were also few in the TURP group. Impotence (8.6%), ejaculation disorder (6.9%), neoplasm non-specific and urgency (5.2%) were the most common adverse events ongoing after 12 months. There was one patient (1.7%) each with PSA increase, urethral disorder, tether stricture and urethral incontinence.

Serious Adverse Events

A Serious Adverse Event was defined as any untoward medical occurrence that:

- resulted in death
- was life-threatening
- required in-patient hospitalization or prolongation of existing hospitalization
- resulted in persistent or significant disability or incapacity
- was cancer
- required intervention to prevent permanent damage to body function or structure.

PLFT-group

The following table identifies all the Serious Adverse Events (SAE) reported for patients treated with PLFT in Study A, Study B and Study C during the 12 month follow-up period (possibly/probably related or non-related to PLFT).

Table 3:

Event	Number	Rate	Causality
Appendicitis	1	0.5%	Non-related
Back pain	1	0.5%	Non-related
Fever	1	0.5%	Related
Heart disorder	1	0.5%	Non-related
Dizziness	1	0.5%	Non-related
Vertigo	2	1.1%	1 Related
Faeces discoloured	1	0.5%	Non-related
Hemorrhoids thrombosed	1	0.5%	Related
Fibrillation atrial	1	0.5%	Non-related
Tachycardia ventricular	1	0.5%	Non-related
Spondylitis ankylosing	1	0.5%	Non-related
Angina pectoris	1	0.5%	Non-related
Angina pectoris aggravated	1	0.5%	Non-related
Myocardial infarction	3	1.6%	Non-related
Neoplasm malignant	1	0.5%	Non-related
Neoplasm non-specific	2	1.1%	Non-related
Epididymitis	1	0.5%	Related
Sepsis	1	0.5%	Related
Pneumonia	1	0.5%	Non-related
Post-operative hemorrhage	1	0.5%	Related
Spinal cord compression	1	0.5%	Non-related
Hematuria	2	1.1%	1 Related
Urethral disorder (perforation)	1	0.5%	Related
Urethral stricture	1	0.5%	Related
Urinary incontinence	1	0.5%	Related
Urinary retention	3	1.6%	2 Related
Cerebrovascular disorder	1	0.5%	Non-related
Haemorrhage intracranial	1	0.5%	Non-related

In total 41 SAEs were reported for the three studies. 6 of the events occurred during the screening period (i.e. pre-treatment).

In the Study A a total of 21 SAEs were reported. Out of these 21 SAEs the investigator judged three to be probably or possibly related to the study treatment; hematuria, post-operative hemorrhage and urethral disorder (perforation).

The perforation occurred prior to treatment during the catheterization and no microwave treatment was performed.

In Study B a total of 13 SAEs were reported. Six out of these 13 SAEs were judged to be probably or possibly related to the study treatment; fever, urinary incontinence, hemorrhoids thrombosed, urethral stricture and two cases with urinary retention.

In Study C, a total of 7 SAEs were reported. Four out of these 7 SAEs were judged to be probably or possibly related to the study treatment; vertigo, sepsis, epididymitis and flare up of epididymitis.

In Study A, one patient had a myocardial infarction that resulted in death 12 month post treatment. The event was assessed as unlikely related to treatment.

No deaths were reported in the other studies.

TURP-group

The following table identifies all the Serious Adverse Events (SAE) reported for patients treated with TURP in Study A and B during the 12 month follow-up period (possibly/probably related or non-related to TURP).

Table 4:

Event	Number	Rate	Causality
Cardiac failure	1	1.5%	Non-related
Diverticulitis, colonic	1	1.5%	Non-related
Arrhythmia	1	1.5%	Non-related
Fibrillation atrial	1	1.5%	Non-related
Gout	1	1.5%	Related
Hypokalemia	1	1.5%	Non-related
Hyponatremia	1	1.5%	Non-related
Myocardial infarction	1	1.5%	Non-related
Colon carcinoma	1	1.5%	Non-related
Neoplasm non-specific	2	3.1%	Non-related
Delirium	1	1.5%	Related
Anemia	1	1.5%	Non-related
Orchitis	1	1.5%	Related
Sepsis	1	1.5%	Related
Post-operative hemorrhage	2	3.1%	Related
Hematuria	3	4.6%	Related

Table 4:

Event	Number	Rate	Causality
Urethral stricture	1	1.5%	Related
Urinary tract infection	1	1.5%	Related
Cerebral hemorrhage	1	1.5%	Non-related
Transient ischemic attack	1	1.5%	Non-related

In total 24 SAEs were reported for the both studies. Three of the events occurred during the screening period (i.e. pre-treatment).

In Study A a total of 19 SAEs were reported. Nine out of these 19 SAEs were judged to be probably or possibly related to the study treatment: gout, delirium, sepsis, post-operative hemorrhage (2), hematuria (3) and urinary tract infection.

In Study A, two deaths were reported in the TURP group. One patient had a myocardial infarction that resulted in death. The event was assessed as unlikely related to treatment.

The other patient died due to a combination of acute myocardial infarction, congestive heart failure and arrhythmia. The event was assessed by the Investigator as possibly related to the treatment.

In the Study B a total of five SAEs were reported. Out of these five SAEs the investigator judged two to be probably or possibly related to the study treatment; orchis and urethral stricture.

No deaths were reported in Study B

Clinical Trial Summary

Study Design

Clinical Protocol under an IDE: Study A

Study A was prospectively planned and was conducted under an IDE at ten centers in Scandinavia and the USA. The original ProstaLund® Standard (PLS) device was used. PLFT was compared to TURP (Trans Urethral Resection of the Prostate). The treatment allocation was double-blind and sealed randomization envelopes were used. Approximately 150 patients with BPH were planned for enrollment to either PLFT or TURP, using a randomization ratio of 2:1 (with twice as many patients in the PLFT group).

The patients were seen at screening (0–6 weeks pre-treatment), at treatment (day 1) and at follow-up visits at 3, 6 and 12 months post-treatment. After study completion the patients will be followed-up on a long-term basis up to 5 years post-treatment. The latter results will be documented and reported separately and submitted to FDA in the beginning of 2005.

The primary objective was the subjective improvement of PLFT compared to TURP after 12 months, in patients with BPH. The primary efficacy variable was the International Prostate Symptom Score (IPSS), which is commonly used when evaluating patients with BPH.

The statistical hypothesis was to test for non-inferiority of treatment with PLFT as compared to TURP using IPSS as the primary variable. One-sided confidence intervals (95%) for the difference in IPSS between PLFT as compared to TURP according to the t-distribution are presented, including the change from baseline. Noninferiority of PLFT as compared to TURP could be claimed if the one-sided 95% confidence interval of the treatment difference in IPSS of PLFT as compared to TURP is 125% or less.

The same principle of statistical analysis was stated also for the secondary variable Q_{\max} . A higher value for Q_{\max} indicated a better response; hence a lower one-sided 95% confidence interval within 80% of PLFT as compared to TURP represented the statistical target.

The responder rate was regarded as a secondary variable. Noninferiority in responder rate for PLFT as compared to TURP could be claimed if the 95% one-sided confidence interval for the difference in the proportion of responders is not lower than 20% of the proportion responders in the TURP group. Calculations according to the t-distribution were used.

A responder was defined as:

- IPSS of 7 or less, and/or
- 50% or greater improvement in IPSS from baseline, and/or
- Q_{\max} of 15 ml/s or more, and/or
- 50% or greater improvement in Q_{\max} from baseline.

If there was data missing at the one-year visit in the responder analysis results from the previous visit replaced the missing value ("last observation carried forward", LOCF).

Secondary objectives were to study the clinical efficacy in terms of objective improvement, as well as to study the safety of PLFT compared to TURP after 12 months regarding:

- max urinary free flow rate (Q_{\max});
- detrusor pressure [at maximum flow rate (P_{det} at Q_{\max})] (as measured by urodynamics);
- residual urine volume;
- prostate volume (as determined by TRUS);
- post-treatment indwelling catheter time;
- adverse events;
- sexual function (i.e. query regarding penetrating coitus and ejaculation ability);
- distribution of patients into responder and non-responder groups.

Supportive Clinical Protocols: Study B and Study C

Study B and C were conducted at single centers in Switzerland and in the Netherlands, respectively. In both cases the subject device ProstaLund® CoreTherm™ was used. These studies were conducted to support the clinical data of Study A performed on the original ProstaLund® Standard (PLS) to ensure outcomes of both devices were comparable.

Study B

Study B was prospectively planned and was conducted at one center in Switzerland. PLFT was compared to TURP. The treatment allocation was double blind and sealed randomization envelopes were used. It was intended to enroll 51 patients with BPH to treatment with either PLFT or TURP, using a randomization ratio of 2:1.

The patients were seen at screening (0-6 weeks pre-treatment), at treatment (day 1) and at follow-up visits at 3, 6 and 12 months post-treatment.

The primary objective was to study the clinical efficacy of PLFT as compared to TURP in patients with BPH in terms of the proportion of responders (see study A for definition) after 12 months of treatment.

The responder rate was regarded as the primary variable. The Objective of the study was to demonstrate that the proportion responders in the PLFT group had a 95% one-sided confidence interval that was not lower than 70%, furthermore, noninferiority of PLFT as compared to TURP was tested by the same principle as in study A. For the secondary variables IPSS and Q_{\max} 95% one-sided confidence intervals for the treatment difference were calculated, and noninferiority of PLFT as compared to TURP tested as in study A.

Secondary objectives were to study the clinical efficacy in terms of subjective and objective improvement, as well as to study the safety of PLFT using TURP as a reference after 12 months regarding:

- IPSS;
- Q_{\max} ;
- detrusor pressure [at maximum flow rate (P_{det} at Q_{\max})] (as measured by urodynamics);
- residual urine volume;
- prostate volume (as determined by TRUS);
- adverse events;

- post-treatment indwelling catheter time;
- sexual function (i.e. query regarding penetrating coitus and ejaculation ability).

Study C

Study C was also prospectively planned and was conducted at one center in the Netherlands. It was intended to evaluate PLFT in 35 patients with BPH. There was no reference group.

The patients were seen at screening (0–4 weeks pre-treatment), at treatment (day 1) and at follow-up visits at 3, 6 and 12 months post-treatment.

The primary objective was to study the clinical efficacy of PLFT in patients with BPH in terms of the proportion of responders (see study A for definition) after 12 months of treatment.

The responder rate was regarded as a primary variable. This study had no comparative group, and the statistical hypothesis was to test, if the proportion responders in the PLFT group had a 95% one-sided confidence interval that was not lower than 70%. Secondary objectives were identical to those established under Study B.

Patient Classification

Patients were classified into a Per-Protocol (PP) sample and an Intention-to-Treat (ITT) sample. The ITT sample represented all patients treated, and the PP sample represents patients who had no major violations* to visit schedules or protocol procedures.

**Major violation was defined as:*

- *patients who at inclusion had, or during the study developed withdrawal criteria but were not withdrawn*
- *patients who had too short wash-out period of 5-alpha reductase inhibitors or alpha blockers prior to treatment*

In addition, patients were excluded from the PP analysis if three or more of the following deviations occurred;

- *one or more missing visits 3-5,*
- *patients who had too long screening period*
- *patients with a too old IPSS result at baseline*
- *patients who had missing IPSS at visit 1 or 3-5*
- *patients who have been seen significantly early or late for one or more of their post treatment visits*

Patient Selection and Exclusion Criteria

The same patient inclusion and exclusion criteria were used in all three clinical study protocols (except for three minor differences in the definitions in exclusion criteria 5, 8 and 14).

Inclusion Criteria

- 1 Patients 45 years or older.
- 2 Symptomatic BPH.
- 3 IPSS ≥ 13 .
- 4 Prostate size: 30-100 g.
- 5 $Q_{\max} < 13$ ml/s on a voided volume > 125 ml.
- 6 Informed consent.

Exclusion Criteria

- 1 Medically and/or psychologically unable to tolerate procedures.
- 2 Previous microwave thermotherapy, TURP, laser prostatectomy or other surgical treatment of the prostate.
- 3 Previous pelvic irradiation or radical pelvic surgery.
- 4 History of urethral strictures, bladder neck contracture, or potentially confounding bladder pathology.
- 5 Evidence of prostatitis.
- 6 Prostatic Specific Antigen (PSA) > 10 mg/l.
- 7 Evidence of prostate cancer or bladder cancer.
- 8 Evidence (as determined by cystoscopy) of median lobe.
- 9 Neurogenic bladder and/or sphincter abnormalities.
- 10 Symptomatic UTI at time of treatment.
- 11 Indwelling catheter or on self-catheterisation.
- 12 Concomitant medication with 5-alpha reductase inhibitors, alpha blockers, anticholinergics, androgens, and gonadotropin-releasing hormonal analogs within 6 weeks of treatment.
- 13 Residual urinary volume > 300 ml.
- 14 Acontractile or hypocontractile detrusors.
- 15 Moderate to severe renal failure (defined as level twice the upper limit of the reference range for the serum creatinine (S-Cr) concentration).
- 16 Patients interested in future fertility.

Demographic Data and Baseline Characteristics

In terms of demographics, medical history, concurrent diseases and other baseline characteristics, both treatment groups (PLFT and TURP) in Study A and Study B were considered to be comparable.

At baseline, mean patient age ranged from 65 to 69 years, mean IPSS from 19.2 to 21.9 and mean Q_{\max} from 7.0 to 8.4 ml/s in the different study groups. Mean prostate volume for the PLFT group in both Study A and Study B was somewhat smaller (48.9 and 51.9 ml, respectively) than that for the PLFT group in Study C (58.3 ml). Mean detrusor pressure [P_{\det} at Q_{\max}] for the PLFT group was slightly higher for Study B (80.9 cmH₂O) as compared to Study A and, in particular, Study C (73.7 and 67.5 cmH₂O, respectively).

Table 5: Demographic data and baseline characteristics in Study A, B and C

Variable (unit)	Mean				
	Study A		Study B		Study C
	PLFT (n = 100)	TURP (n = 46)	PLFT (n = 42)	TURP (n = 19)	PLFT (n = 41)
Age (years)	67	69	67.5	67.7	65
Weight (kg)	83	81	80	82	80

Table 5: Demographic data and baseline characteristics in Study A, B and C

Variable (unit)	Mean				
	Study A		Study B		Study C
	PLFT (n = 100)	TURP (n = 46)	PLFT (n = 42)	TURP (n = 19)	PLFT (n = 41)
Height (cm)	178	177	175	175	178
Prostate volume [by TRUS] (ml)	48.9	52.7	51.9	56.0	58.3
PSA (µg/l)	3.3	3.6	4.3	4.6	3.4
IPSS	21.0	20.4	20.0	19.2	21.9
Q _{max} (ml/s)	7.6	7.9	7.0	7.0	8.4
Detrusor pressure [P _{det} at Q _{max}] (cmH ₂ O)	73.7	79.4	80.9	79.8	67.5

Number of centers and study population

Ten centers, six in Sweden, two in Denmark and two in the USA participated in Study A. A total of 154 patients were randomized and 146 were treated. At 12 months, 133 patients had completed the study and 13 patients had been withdrawn (nine in the PLFT group and four in the TURP group).

One center in Switzerland participated in Study B. A total of 62 patients were randomized and 61 were treated. At 12 months, 55 patients had completed the study and six patients had been withdrawn (three in the PLFT group and three in the TURP group).

One center in the Netherlands participated in Study C. A total of 42 patients were enrolled and 41 were treated. At 12 months, 33 patients had completed the study and eight patients had been withdrawn.

Table 6: Centers and number of patients in study A, B and C

Country	Center no. & city	Patients enrolled/included:			
		In total	PLFT	TURP	SF*
– Study A					
Sweden	01. Uppsala	33	21	11	1
	02. Hudiksvall	19	11	6	2
	03. Lund	18	11	6	1
	04. Ljungby	15	9	3	3
	05. Kristianstad	21	15	6	-
	06. Kalmar	25	17	8	-
Denmark	07. Frederiksberg	7	5	2	-

Table 6: Centers and number of patients in study A, B and C

Country	Center no. & city	Patients enrolled/included:			
		In total	PLFT	TURP	SF*
The USA	08. Herlev	5	3	2	-
	09. Scottsdale, AZ	3	3	-	-
	10. Toledo, OH	8	5	2	1
Total number of patients in Study A:		154	100	46	8
– Study B					
Switzerland	13. Aarau	62	42	19	1
– Study C					
The Netherlands	14. Nijmegen	42	41	na**	1
Total number of patients:		258	183	65	10

*) Screening Failure not treated (i.e. withdrawn before treatment but after allocation of a randomization/patient number)

**) There was no control group in Study C.

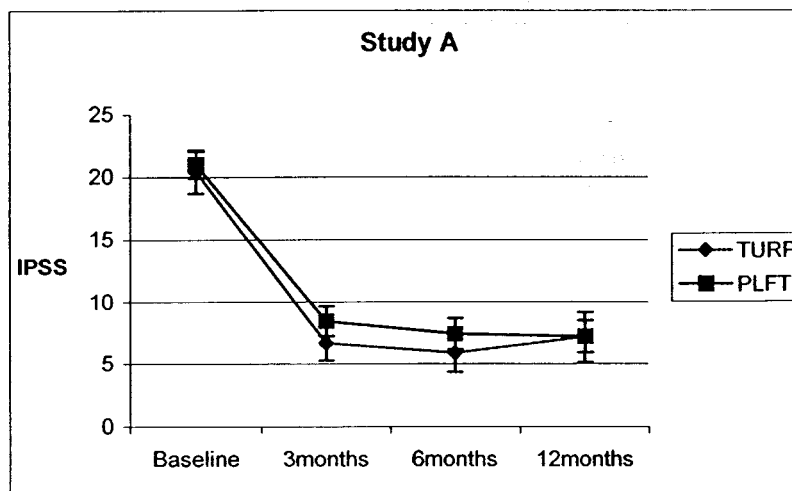
Study Period

The three studies were conducted during the period October 1998 to October 2001. Study A will continue in a long-term follow-up study up to 5 years post treatment.

Data Analysis and Results

Study A

There was a marked post-treatment decrease in IPSS at the 3-month follow-up visit both in the PLFT and TURP groups (see graph below). The decrease in IPSS was maintained up to 12 months post-treatment for both groups.



Mean IPSS values and 95% confidence intervals for PLFT and TURP data in study A.

The ITT analysis demonstrated the ratio PLFT to TURP for mean IPSS was 113.2% with an one-sided 95% confidence interval of 137.0%. The statistical target set was $\leq 125\%$. Results were similar when the baseline-adjusted IPSS were considered as well as the results for the PP analysis. Analysis of the percent responders are presented below for the ITT and PP data.

Table 7: Responders at 12 months follow-up – ITT analysis

Study	Percentage of responders, LOCF (95% confidence interval)		Difference (PLFT – TURP)	One-sided 95% confidence interval (CI) for difference
	PLFT (n=100)	TURP (n=46)		
Study A	82.0% (74.4% – 89.6%)	87.0% (77.0% – 97.0%)	-5.0%	CI: -15.4%

Table 8: Responders at 12 months follow-up – PP analysis

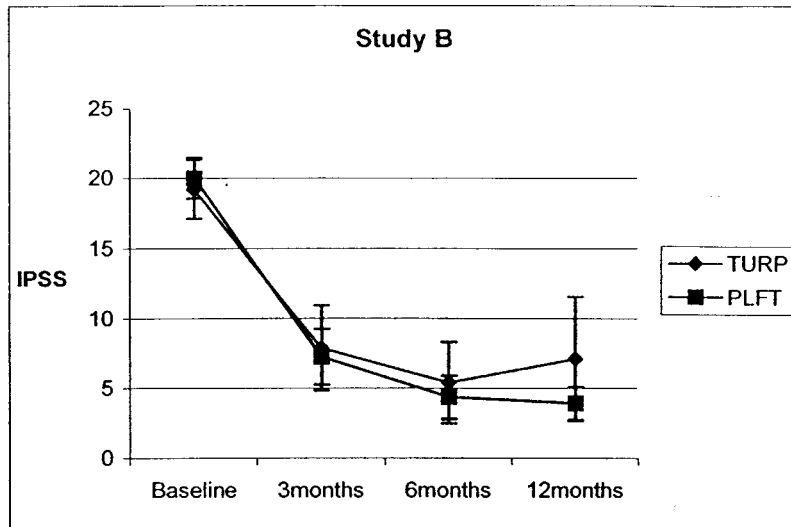
Study	Percentage of responders, LOCF (95% confidence interval)		Difference (PLFT – TURP)	One-sided 95% confidence interval (CI) for difference
	PLFT (n=93)*	TURP (n=42)*		
Study A	82.8% (75.0% – 90.6%)	88.1% (78.0% – 98.2%)	-5.3%	CI: -15.8%

- One patient in each group with missing data (patients withdrawn due to adverse events) excluded from PP sample (PLFT: patient withdrawn due to prostate cancer; TURP: patient expired)

Mean Q_{max} improved from a baseline value of 7.6 ml/s to 13.3 ml/s at 12 months for the PLFT group. In comparison, mean value for the TURP group improved from 7.9 ml/s to 15.2 ml/s. The ITT analysis demonstrated the ratio PLFT to TURP for mean Q_{max} was 93.3% with an one-sided 95% confidence interval of 80.9%, which was within the statistical target of $\geq 80\%$. For the baseline adjusted Q_{max} the ratio for PLFT to TURP was similar (92.4%), but the one-sided confidence interval slightly lower than 80% (78.3%). Results of the PP analysis were in accordance with these data.

Study B

In accordance with results seen in study A, IPSS improved for both treatment groups post-treatment (see graph below). The decrease in IPSS was maintained up to 12 months post-treatment for both groups.



Mean IPSS values and 95% confidence intervals for PLFT and TURP data in study B.

The ITT analysis demonstrated the ratio PLFT to TURP for mean IPSS was 80.3% with a one-sided 95% confidence interval of 111.4%. The statistical target set was $\leq 125\%$. Results were similar when the baseline-adjusted IPSS were considered as well as the results for the PP analysis. Analysis of the percent responders are presented below for the ITT and PP data.

Table 9: Responders at 12 months follow-up – ITT analysis

Study	Percentage of responders, LOCF (95% confidence interval)		Difference (PLFT – TURP)	One-sided 95% confidence interval (CI) for difference
	PLFT (n=42)	TURP (n=19)		
Study B	88.1% (78.0% – 98.2%)	79.0% (59.3% – 98.6%)	9.2%	CI: -8.6%

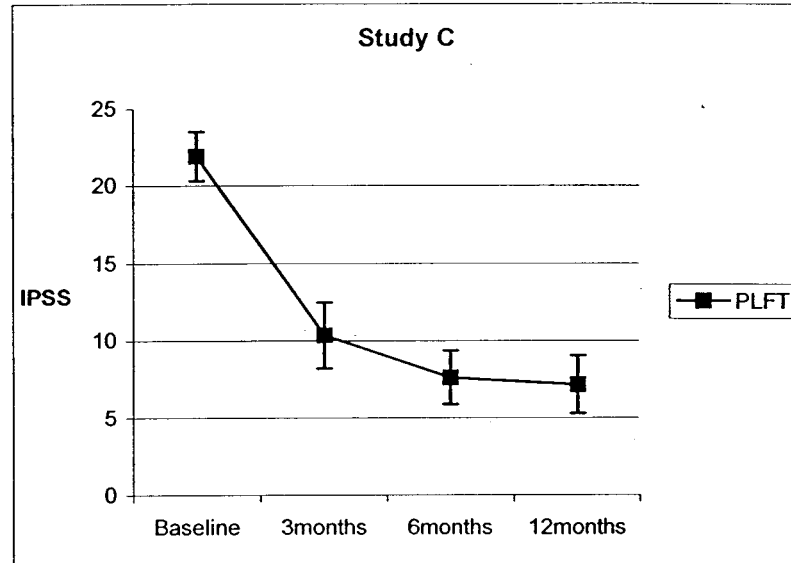
Table 10: Responders at 12 months follow-up – PP analysis

Study	Percentage of responders, LOCF (95% confidence interval)		Difference (PLFT – TURP)	One-sided 95% confidence interval (CI) for difference
	PLFT (n=40)	TURP (n=17)		
Study B	92.5% (84.1% – 100.9%)	82.4% (62.7% – 102.0%)	10.2%	CI: -6.8% - 27.1%

Mean Q_{\max} improved from a baseline value of 7.0 ml/s to 19.9 ml/s at 12 months for the PLFT group. In comparison, mean value for the TURP group improved from 7.9 ml/s to 25.2 ml/s. The ITT analysis demonstrated the ratio PLFT to TURP for mean Q_{\max} was 69.9% with a one-sided 95% confidence interval of 54.6%, which was not within the statistical target of $\geq 80\%$. Results for the baseline adjusted Q_{\max} the ratio for PLFT to TURP and the PP analysis were in accordance with these data.

Study C

In accordance with results seen in study A, IPSS improved post-treatment (see graph below). The decrease in IPSS was maintained up to 12 months post-treatment.



Mean IPSS values and 95% confidence intervals for PLFT in study C.

Table 11: Responders at 12 months follow-up – ITT analysis

Study	Percentage of responders, LOCF (95% confidence interval)	One-sided lower 95% confidence interval
	PLFT (n=41)	PLFT (n=41)
Study C	80.5% (68.0% – 93.0%)	70.1%

Table 12: Responders at 12 months follow-up – PP analysis

Study	Percentage of responders, LOCF (95% confidence interval)	One-sided lower 95% confidence interval
	PLFT (n=37)	PLFT (n=37)
Study C	86.5% (75.1% – 97.9%)	77.0%

Mean Q_{\max} improved from a baseline value of 8.4 ml/s to 17.8 ml/s at 12 months for the patients in this study.

Summary Study A, B and C

IPSS

In all three studies and in each of the treatment groups, there was a decrease in IPSS at the 3-month follow-up. At 12 months post-treatment, mean scores of IPSS for the PLFT group in Study A, Study B and Study C had decreased significantly as compared to baseline (see graphs). This was also seen for the TURP group in Study A and Study B.

Responders to Treatment

As can be seen in the tables, patients in the PLFT group had responder rates that were comparable to those in the TURP group. Data for PLFT patients in Study C were in agreement with results in Study A and Study B. There were no major differences seen between the PP and ITT sample of patients.

Responder rate and percentage of patients with 50% or greater improvement in IPSS, or IPSS and Q_{\max} , at 12 months follow-up in the ITT sample are shown below.

Table 13:

Study	Percentage and number (n) of responders, LOCF	
Study A	PLFT N=100	TURP N=46
Responders (overall definition)	82.0% (82/100)	87.0% (40/46)
50% or greater improvement from baseline in IPSS	71.0% (71/100)	71.7% (33/46)
50% or greater improvement from baseline in both IPSS and Q_{\max}	34.0% (34/100)	39.1% (18/46)
Non responders*	18.0% (18/100)	13.0% (6/46)
Study B	PLFT N=42	TURP N=19
Responders (overall definition)	88.1% (37/42)	79.0% (15/19)
50% or greater improvement from baseline in IPSS	85.7% (36/42)	73.7% (14/19)
50% or greater improvement from baseline in both IPSS and Q_{\max}	81.0% (34/42)	63.2% (12/19)
Non responders	11.9% (5/42)	21.1% (4/19)
Study C	PLFT N=41	**
Responders (overall definition)	80.5% (33/41)	-
50% or greater improvement from baseline in IPSS	65.9% (27/41)	-
50% or greater improvement from baseline in both IPSS and Q_{\max}	51.2% (21/41)	-
Non responders*	19.5% (8/41)	-

- Non-responders included also a few patients with missing data for both IPSS and Q_{\max}
- ** Study C had no control group

Other Secondary variables**Bother score**

In accordance, the results of bother score indicated a pronounced improvement in all study treatment groups. From baseline to 12 months after treatment, mean bother score for the PLFT group in Study A, Study B and Study C decreased with 67, 78 and 68%, respectively (i.e. went from 4.3, 3.7 and 4.2 to 1.4, 0.8 and 1.4, respectively). For the TURP group in both Study A and Study B, the decrease in mean bother score was 64 and 65%, respectively (i.e. change from 4.2 and 3.7 to 1.5 and 1.3, respectively).

Detrusor pressure

Mean detrusor (voiding) pressure [at max urinary flow rate (P_{\det} at Q_{\max})] decreased from baseline to 12 months with 34 and 47% for the PLFT and TURP groups in Study A, respectively (i.e. decreased from 73.8 to 48.4 cm H_2O in the PLFT group and from 79.4 to 41.8 cm H_2O in the TURP group). In Study B the mean detrusor pressure decreased from baseline to 12 months from 80.9 to 46.7 cm H_2O in the PLFT group and from 79.8 to 42.3 cm H_2O in the TUR-P group. In Study C the detrusor pressure decreased from 67.5 to 62.6 cm H_2O in the PLFT group.

Prostate volume

Mean prostate volume as determined by TRUS for the PLFT group in Study A, Study B and Study C was 48.9, 51.8 and 58.3 ml at baseline and 34.2 ml, 32.2 and 36.4 ml at 12 months, respectively. The corresponding relative changes were 30, 38 and 38%, respectively. For the TURP group in Study A and Study B, mean prostate volume as measured by TRUS decreased with 51 and 64%, respectively (i.e. went from 52.7 and 56.0 ml to 25.6 and 20.2 ml at 12 months, respectively).

Post-treatment indwelling catheter time

The mean post-treatment indwelling catheter time was 14, 20 and 18 days for the PLFT group in Study A, Study B and Study C, respectively. For the TURP groups it was shorter i.e. 3.1 days in both Study A and Study B, as expected due to the two different types of intervention (coagulation vs. resection of prostate tissue).

Information for Patients

Information for Patients Physicians should inform patients that an inherent risk of complications is associated with PLFT (refer to adverse events). Patients should be informed that they might experience the following adverse events (sorted by frequency, from the most common event to the least common event, based on 12 month follow-up):

- Urgency
- Urinary tract infection
- Urinary retention
- Bladder spasm
- Hematuria
- Suprapubic and general pain including penile pain
- Dysuria
- Ejaculation disorder (retrograde ejaculation)
- Impotence
- Micturition frequency
- Urinary incontinence
- Epididymitis
- Hypertension
- Prostatitis
- Urethral stricture
- Hypotension
- Bleeding

Patients should also be informed that they need to have an indwelling catheter for 1-3 weeks after the treatment.

Patients should be informed that possible side effects of thermotherapy treatments could include the adverse events listed below. However, these side effects were not experienced during the clinical studies of PLFT:

- Rectal damage/fistula
- Burn injuries outside the treatment area
- Incontinence caused by injuries to the external sphincter

CoreTherm[®] Microwave Thermotherapy

Patient Information

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Glossary

Words that are included in the glossary are designated by an asterisk* when used in the text throughout the patient information.

ANESTHESIA:

- **Conscious Sedation** – Medications used to make you sleepy, decrease anxiety, increase relaxation, and pain control during medical procedures. Can be easily awakened with touch or voice to communicate with the doctor
- **Local anesthesia** – Medication delivered locally, either injected or topical, to produce a loss of sensation at a specific site

Antibiotic – A medicine used to treat or prevent infection

BPH – Benign Prostatic Hyperplasia is a non-cancerous enlargement of the prostate that can cause pressure on the urethra*, making it more difficult to empty the bladder.

CATHETER:

- **Drainage Catheter** – A flexible tube for withdrawing urine from the bladder through the urethra into a urine collection bag.
- **Treatment Catheter** – A flexible tube placed in the bladder through the urethra that is used to hold the probe for monitoring the temperature in the prostate and the microwave treatment device.

Ejaculation – A sudden release of semen from the urethra* during orgasm

Fertility – The ability to produce sperm

Impotence or Erectile Dysfunction – The inability to achieve penile erection or to maintain an erection until ejaculation.

Microwave energy – high frequency electrical energy that causes heat

Minimally Invasive Procedure – Treatment through a natural body opening such as the penis.

Prostate – a body around the base of the male urethra that is part muscle and part gland and produces a secretion that is a major part of the fluid given off usually during an orgasm.

Retrograde ejaculation – semen is deposited into the bladder during orgasm instead of being expelled through the penis

Thermotherapy – treatment that uses high temperatures to destroy tissue

Urethra – the tube through which urine is passed from the bladder

Urinate – the act of passing urine from the bladder

The CoreTherm® Microwave Thermotherapy* Treatment

GENERAL DESCRIPTION

The CoreTherm® Microwave Thermotherapy* treatment, is a minimal invasive treatment* for benign prostatic hyperplasia (BPH*), a non-cancerous condition in men. The treatment uses microwave energy* to heat the prostate* destroying some of the tissue to reduce pressure on the urethra*. The energy travels through a special treatment catheter* that is inserted into the urethra*. CoreTherm® treatment uses a unique, patented technology that enables the doctor to continuously measure the temperature in the prostate and customize the treatment to each patient's individual needs. There are also safety temperature sensors used to ensure a safe procedure.

Three clinical studies of CoreTherm® Microwave Thermotherapy have been performed, in which the primary objective was to study the clinical efficacy in patients with symptomatic BPH after a 12-month follow up. Study A showed that the CoreTherm Microwave Thermotherapy and TURP produced results in the same range for all the efficacy variables: IPSS, bother score, Q_{max} , detrusor pressure and residual urine volume. Thus, PLFT was able to show the same improvements as those seen after TURP in both subjective and objective efficacy variables after 12 months follow up. The one-year effectiveness results for PLFT demonstrate the durability of the treatment response. The results reported from the studies B and C showed that the CoreTherm® Microwave Thermotherapy provides an effective and safe treatment with results similar to those seen in study A.

CoreTherm® Microwave Thermotherapy* may be performed in your doctor's office or in a hospital out patient department. The procedure typically takes between 15 and 70 minutes. This procedure generally does not require a hospital admission and is usually performed using conscious sedation* and a local anesthetic* to make you more comfortable. Clinical studies show that more than 80 percent of patients experience a definite improvement within three to six months.

Benign prostatic hyperplasia, known as BPH* or enlarged prostate*, is a non-cancerous condition that frequently causes an abnormal flow of urine in men over 50 years of age. Around 25 percent of all men receive some kind of treatment for BPH* before the age of 80. Since the symptoms of other diseases can be similar to BPH*, it is important that you see your doctor. He or she can accurately diagnose what is causing your symptoms—and recommend the best treatment for you.

Your doctor is the best resource for answers to all your questions about BPH*, including the choices for treatment and the advantages and disadvantages of each treatment option. Be sure to talk to him or her to determine which treatment is best for you.

TREATMENT OPTIONS:

You should discuss these with your doctor.

- Watchful Waiting
- Drug Therapy
- Surgery

POTENTIAL COMPLICATIONS WITH THIS PROCEDURE

CoreTherm® Microwave Thermotherapy* treatment is considered a safe and effective treatment with a low risk of complications. However, like any treatment, there may be complications or side effects. These complications are similar to the complications reported after surgery, drug therapy, and other non-invasive treatments currently used to treat BPH.

There is an inherent risk of complications associated with microwave thermotherapy. In most cases, the events were of mild or moderate intensity. Most adverse events were resolved within a short period (average 11 days). The list below provides the reported adverse events observed during the clinical studies with CoreTherm, the adverse events are sorted by frequency from the most common event to the least common event based on 12 months follow up.

- Urgency
- Urinary tract infection
- Urinary retention
- Bladder spasm
- Hematuria
- Suprapubic and general pain including penile pain
- Dysuria
- Ejaculation disorder (retrograde ejaculation)
- Impotence*
- Micturition frequency
- Urinary incontinence
- Epididymitis
- Hypertension
- Prostatitis
- Urethral stricture
- Hypotension
- Bleeding

During the clinical studies with CoreTherm, some patients reported ongoing symptoms 12 months after treatment including, bladder spasm, hematuria, prostatitis, pain, urinary tract infection, urinary incontinence, urinary frequency, urinary urgency, and/or urethral stricture.

Other adverse events that have not been reported with the CoreTherm but may occur with thermotherapy treatment include:

- ✓ Rectal damage/fistula
- ✓ Burn injuries outside the treatment area
- ✓ Incontinence caused by injuries to the external sphincter
- ✓ Sterility and/or Impotence*

TREATMENT PREPARATION AND PROCEDURE

What to do at home before CoreTherm Microwave Thermotherapy*

- You should have a bowel movement shortly before treatment. Take a laxative or Fleet® enema if necessary according to the recommendations of your doctor.
- Your doctor may prescribe a mild sedative* and/or relaxant prior to treatment. Have someone drive you to your appointment and take you home.

What will happen before Treatment

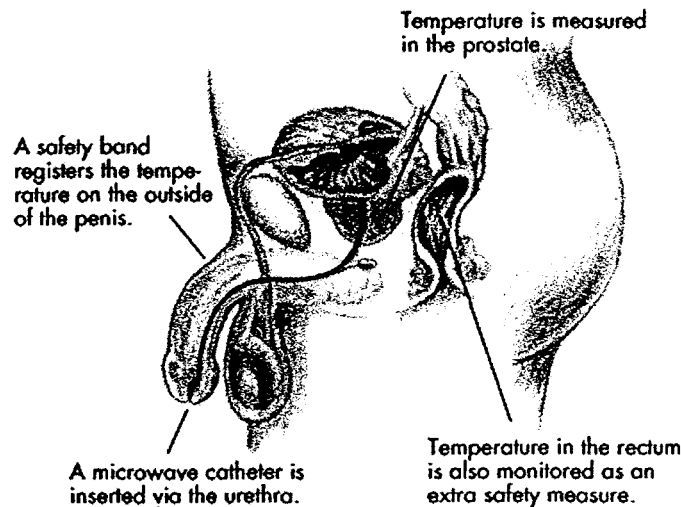
- You will be asked to lie on a treatment table. Your blood pressure, heart rate, and body temperature will be taken. To make you more comfortable, your doctor will administer conscious sedation* either orally or intravenously. Make sure you are comfortable since you will need to remain in this position during the treatment. It is important that you lie still so that the treatment catheter and monitoring devices stay in place throughout the treatment, otherwise there is a risk of getting the therapeutic heat outside the prostate.
- Your physical status including blood pressure, pulse, heart activity and the amount of oxygen in your blood may be observed before during and after the procedure.
- The treatment area will be washed with an antiseptic liquid to decrease the normal germs on the skin.
- A thin tube, called a drainage catheter*, will be placed into your urethra* to empty your bladder before the treatment begins.
- Local anesthesia* will be placed into the urethra* to minimize potential discomfort.
- The treatment catheter*, a special temperature monitoring device (called an intraprostatic thermometer) and the microwave treatment device will be inserted into your urethra*. This should not be uncomfortable however you may feel a small prick.
- A special temperature-monitoring device is inserted into your rectum. A band, which registers temperatures around the base of penis, is attached. These devices assist the doctor in providing a safe procedure and should not cause discomfort.
- The procedure takes between 15 to 70 minutes.

What to expect during Treatment

- Throughout the procedure:
 - Your doctor determines how much tissue needs to be treated to relieve your symptoms.
 - The computer calculates and monitors the amount of prostate tissue treated.
 - During the treatment your doctor monitors eight safety sensors — inside your prostate, inside the rectum and around the base of your penis — to keep the procedure safe and effective.

- During the procedure you may experience some discomfort.
 - Be sure to tell your doctor or nurse about any discomfort. They need to know if you feel heat, pain, the need to urinate, dizziness or any other symptoms. They will try to make the procedure as comfortable as possible for you.
- The treatment is automatically stopped if any temperatures in the prostate*, at the base of the penis, or in the rectum reach the pre-set safety limit.
- The doctor can adjust the heat and/or stop the treatment depending on how your body responds to the treatment.

At the end of the procedure, the treatment catheter is replaced with a drainage catheter attached to a urine collection bag. You may keep the drainage catheter between one to three weeks to allow the prostate to shrink and begin the healing process. Your doctor will determine when to remove this catheter. Your doctor and the staff will teach you how to care for the catheter and empty the drainage bag.



What to expect after Treatment

- You will be allowed to return home shortly after the treatment. Plan to rest for a few days and avoid heavy lifting or strenuous activities. You may not remember having treatment after the procedure after it is over.
- The urethra* and prostate* gland swell during and following the treatment and need time to heal. This may cause discomfort, particularly in the first 24 hours. A catheter is required during the initial healing process.
- Your doctor will prescribe antibiotics* to reduce the possibility of infection. It is important that you take all the medication prescribed. If you develop a rash, stomach or abdominal pain or diarrhea, contact the doctor immediately.
- Your doctor may also prescribe additional medicine that will make you more comfortable.
- Following the treatment you may experience frequent urges to urinate*. You may also experience some aches and pains. These problems will gradually diminish.

- Drink plenty of fluids to minimize the irritation of the catheter and reduce the number of bacteria that could cause infection.
- You may see some blood in your urine or small gray particles. This is completely normal and will go away over time. If the catheter does not appear to be draining or you see of more than a small amount of blood mixed with your urine, you should contact your doctor's office immediately.
- Your doctor will monitor your progress as you continue to get better over several months — even up to a year.

IMPORTANT:

Call your doctor immediately if:

- you pass more than a few drops of blood;
- there is no drainage from the draining catheter and you have a feeling of bladder fullness; and/or
- you have a fever above 101°F

Throughout your recovery, if you have any questions or concerns, be sure to discuss them with your doctor. You can contact your Doctor by phone _____.

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